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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,708	12/20/2001	Michael R. Boyd	213045	9974

23460 7590 10/07/2005

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EXAMINER

MITCHELL, GREGORY W

ART UNIT PAPER NUMBER

1617

DATE MAILED: 10/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/914,708	Applicant(s) BOYD, MICHAEL R.	
	Examiner Gregory W. Mitchell	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 September 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This Office Action is in response to the Remarks, Amendments and Declaration filed September 01, 2005. Claims 1 and 6-7 have been amended. Claims 18-31 have been cancelled. Claims 1-17 are pending and are examined herein.

Applicant's Declaration is sufficient to overcome the 35 USC 103 rejection over Boyd et al., Oku et al., Simon et al., Holt et al. and Yamamoto et al. Applicant's amendments are sufficient to overcome the objection to claims 1 and 6-7. Applicant's arguments regarding the objection to claims 8-11 are persuasive. All rejections and objections of the Office Action dated June 30, 2005 are hereby withdrawn. Prosecution on the merits of the instant application is hereby **REOPENED**.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

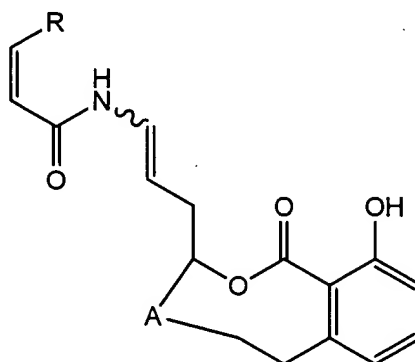
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-7 and 12-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boyd et al. (*J. Org. Chem.*, 63, 7805-10) in view of Oku et al. (WO 99/21835) and Simon et al. (2002/0042079).

Boyd et al. teaches Lobatamindes A-D as having anti-tumor activity. The compounds were found to correlate with compounds

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Boyd et al. teaches Lobatamides A-D as having anti-tumor activity. The Lobatamidine activity was found to correlate with that of Salicylihalamides A and B because of their common core:



See page 7808, last ¶, to page 7809, first ¶ and chart 1, and page 7810, 8th full ¶. Boyd et al. does not teach the administration of the apicularen A or B, the claimed amounts or the treatment of intra-organellar acidification of intracellular organelles, specifically.

Oku et al. teaches malignant tumors (e.g. those related to melanoma and lung cancers) are known to be treatable by vacuolar type H⁺-ATPase inhibition (pp. 15-16).

Simon et al., it is known in the art that the enhanced sensitivity of tumor cells to chemotherapeutics is a consequence of a reduced acidification within the organelles ([0187]).

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer a composition of the Lobatamides, Salicylihalamides or Apicularens claimed in a method of treating a tumor because such compounds a core shared by the claimed compounds are taught to be known in the art as anti-tumor agents. Accordingly the skilled artisan would have been motivated to utilize the claimed

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compounds in a method of treating a tumor because Boyd et al. teaches that compounds with such a core are useful therefor.

It is noted that while other pathways are possible for the treatment of cancers, such as lung tumors, the administration of the compounds of Boyd et al. would obviously meet the claims because Oku et al. teaches that it is known in the art to treat cancers by inhibiting vacuolar type H⁺-ATPase and Simon et al. teaches that it is known in the art to enhance the treatment of cancer by reducing acidification within the organelles. Accordingly, the treatment of, e.g., a lung tumor of Boyd et al. would meet the conditions of "A method of treating an intra-organellar acidification of intracellular organelles by the inhibition of vacular-type (H⁺)-ATPase" because a claim for the administration of the same compound to the same population is not rendered patentable by the discovery of a new mechanism by which the treatment works.

It is noted that claims 12-17 are directed to amounts of compound to be administered. It has been established that "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Claims 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boyd et al., Oku et al. and Simon et al. as applied to claims 6-7 above, and further in view of Holt et al. (WO 93/18652) and Yamamoto et al. (*Cell Struct. Funct.* 1998, **23**, 33-42)

Boyd et al., Oku et al. and Simon et al. apply as disclosed above. The references lack a teaching of bafilomycins and concanamycins.

Holt et al. teaches the administration of bafilomycins (ATPase inhibitors) for the inhibition of cancers (Abstract, p. 2).

Yamamoto et al. teaches that the V-ATPase inhibition activity of bafilomycin A₁ is related to its cause of autophagy in rat hepatoma cell lines (cancer) (Abstract; pp. 33-34 and 40). Yamamoto et al. also teaches the equivalence of the V-ATPase inhibition activities of bafilomycin A₁ and concanamycins (pp. 40-41).

It would have been obvious to one of ordinary skill in the art to add the compounds claimed to a treatment of the combined references because Holt et al. teaches bafilomycins as known in the art to be administered for the inhibition of cancer. Furthermore, it would have been obvious to specifically use bafilomycin A₁ as the bafilomycin or to substitute the bafilomycin with concanamycin A in the treatment rendered obvious by Boyd et al. and Yamamoto et al. because (1) bafilomycin A₁ is a bafilomycin; (2) bafilomycin A₁ is taught by Yamamoto et al. to cause atophagy in cancer cells; (3) concamamycins are taught to be the functional equivalent of bafilomycin A₁ by Yamamoto et al.; and (4) concamamycin A is a concamamycin. "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Response to Arguments /Declaration

The Declaration filed on September 01, 2005 under 37 CFR 1.131 is sufficient to overcome the Boyd et al. (WO 99/05136) reference.

Applicant's arguments are moot in view of the new grounds of rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory W Mitchell whose telephone number is 571-272-2907. The examiner can normally be reached on M-F, 8:30 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

gwm



**SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER**